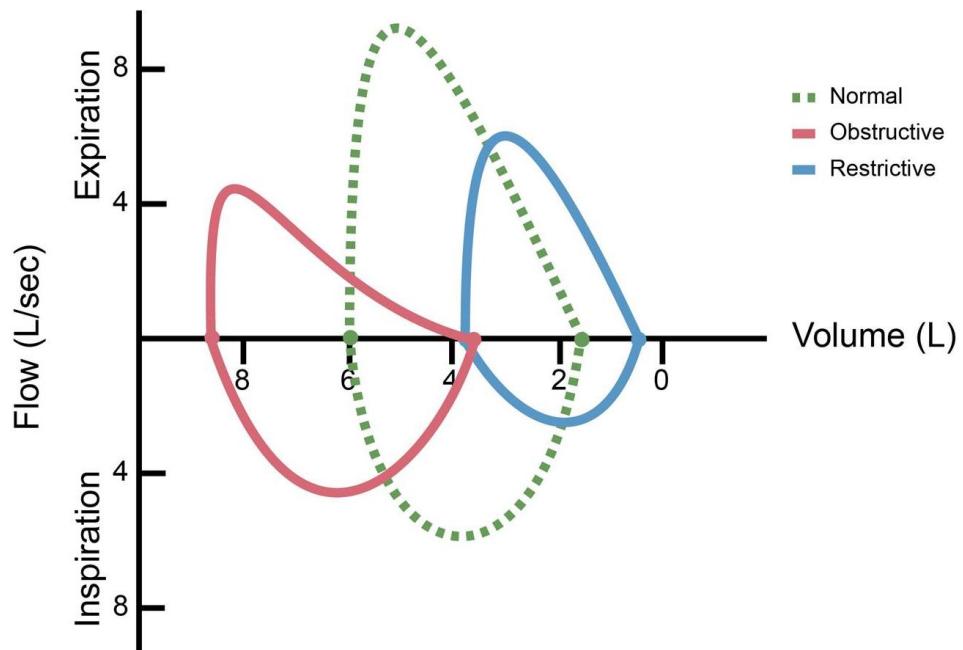




Respiratory System Physiology

Comprehensive File 4 – V1

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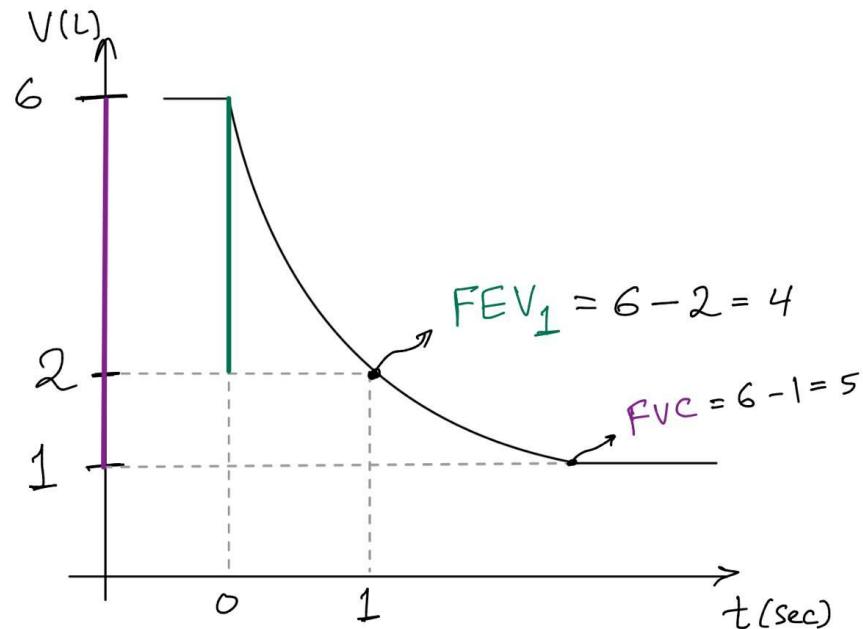
Continuation of Airway Resistance

Lungs are elastic structures that tend to collapse unless expanded by negative intrapleural pressure generated by respiratory muscles. The work of breathing is composed of two main components: elastic work and nonelastic (resistive) work. Approximately 70% of the work is elastic, while 30% is nonelastic.

The elastic component represents the work required to overcome lung elasticity and surface tension in the alveoli. The nonelastic component consists of airway resistance (80%) and tissue viscosity (20%).

This resistance, and therefore the pressure gradient and energy (ATP) required for breathing, has a dynamic component, meaning it increases during airflow, similar to skeletal muscle, which requires more force during movement than during static holding. For example, if the total force needed to overcome the collapsing forces on the lungs is (-6) mmHg, about (-2) mmHg is dynamic, and (-4) mmHg is static. (-) is for outward.

FVC & FEV₁ – Diagnosis of Pulmonary Diseases



Forced Vital Capacity (FVC) is the maximum volume of air that can be forcefully exhaled after a full inspiration. A normal example value is 5 L.

Forced Expiratory Volume in 1 second (FEV₁) is the volume of air exhaled during the first second of forced expiration, reflecting airway resistance. A normal example value is 4 L.

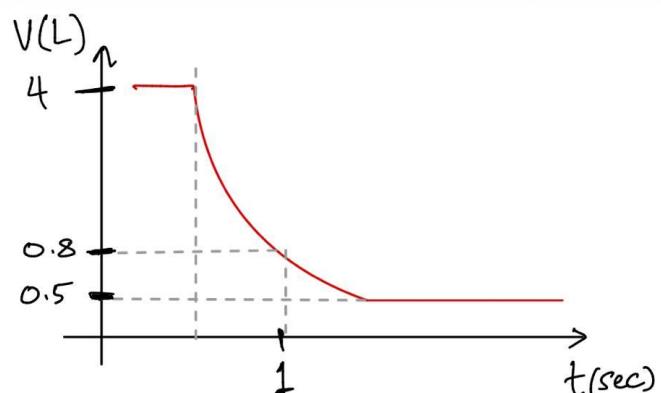
The predicted FEV₁ is calculated using anthropometric data, including age, ethnicity, sex, height and weight. The FEV₁ observed-to-expected ratio (FEV₁ % predicted) should be $\geq 80\%$. Values of 60–79% indicate mild COPD, 40–59% indicate moderate COPD, and $<40\%$ indicate severe COPD. So, airway obstruction is not all-or-none but a gradient.

The FEV₁/FVC Ratio

The FEV₁/FVC ratio represents the fraction of the vital capacity exhaled in the first second and is normally 80% (4 L / 5 L). This ratio is used clinically to identify obstructive lung disease, and a value $<70\%$ indicates airflow obstruction consistent with COPD.

In restrictive lung disease, lung expansion is limited, resulting in a reduced FVC. Both FEV₁ and FVC decrease, but they decrease proportionally, so the FEV₁/FVC ratio remains normal or increased.

Thus, a low FVC with a normal or high FEV₁/FVC ratio suggests a restrictive pattern, rather than obstruction.



For the example above, the FVC is 3.5 L, and the FEV₁ is 3.2, so the ratio is about 91%. The ratio alone assures this is not obstructive disease. It is either normal or restrictive.

To differentiate between normal and restrictive, the absolute numbers are important. Since 3.5 L-FVC is low, this is abnormal, thus it is restrictive lungs disease.

Bronchodilator administration for asthma vs COPD assessment:

Spirometry is first performed before SABA administration. If an obstructive pattern is present (FEV₁/FVC $<70\%$), a short-acting β_2 -agonist (SABA), such as salbutamol or albuterol, is given, and then spirometry is repeated (*results are in the next page*).

- Positive bronchodilator response:
 - $\geq 12\%$ or ≥ 200 mL increase in FEV_1
 - Indicates reversible obstruction, classically asthma
- Negative or minimal response:
 - Little or no improvement in FEV_1
 - Supports fixed obstruction, consistent with COPD

Before confirming COPD, patients with an obstructive spirometric pattern should be treated with glucocorticoids for 2 weeks, after which spirometry is reassessed.

If there is significant improvement in airflow obstruction after the 2-week glucocorticoid course, this indicates reversible airway disease, favoring asthma. If airflow obstruction persists after 2 weeks of glucocorticoid therapy, this indicates fixed airflow limitation, supporting a diagnosis of COPD.

| | Obstr. | Restr. |
|-------------|--------|--------|
| FEV_1 | ↓ | ↓ |
| FVC | →↓ | ↓ |
| FEV_1/FVC | ↓ | →↑ |

The table above summarizes key differences between obstructive and restrictive lung disease in comparison to the normal.

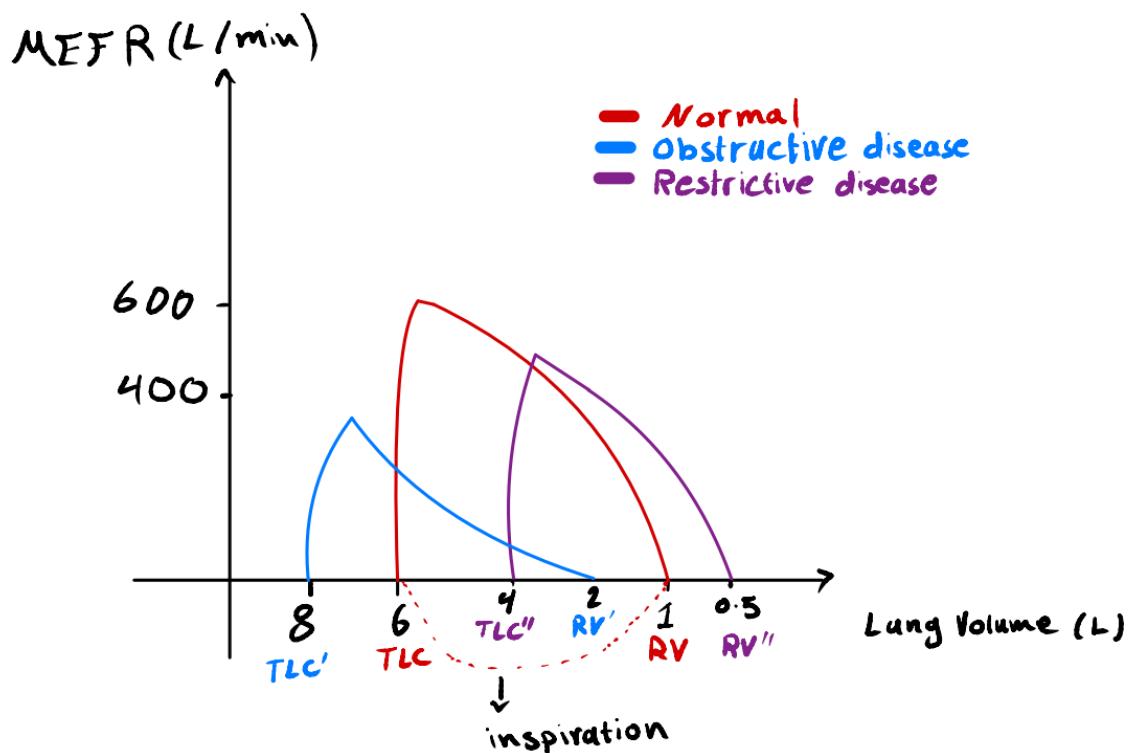
FEV_1 is decreased in obstructive due to absolute inability to fast exhale air. However, it is decreased in restrictive due to overall decrease in all volumes, not due to airway resistance.

FVC can be near normal if the obstructive disease patient is given enough time to exhale all the air present, but FVC is always decreased in restrictive disease.

Algebraic manipulation yields the third row by examining the nature of the fraction.

Maximum Expiratory Flow Rate

The following curve, known as the flow–volume loop, illustrates the measurement of the maximum expiratory flow rate (MEFR). In normal lung function, the measurement starts at total lung capacity (TLC), approximately 6 L, where the expiratory flow rate reaches a maximum value of about 600 L/min (or 10 L/s). As expiration continues, the flow rate progressively decreases and reaches zero at residual volume (RV).



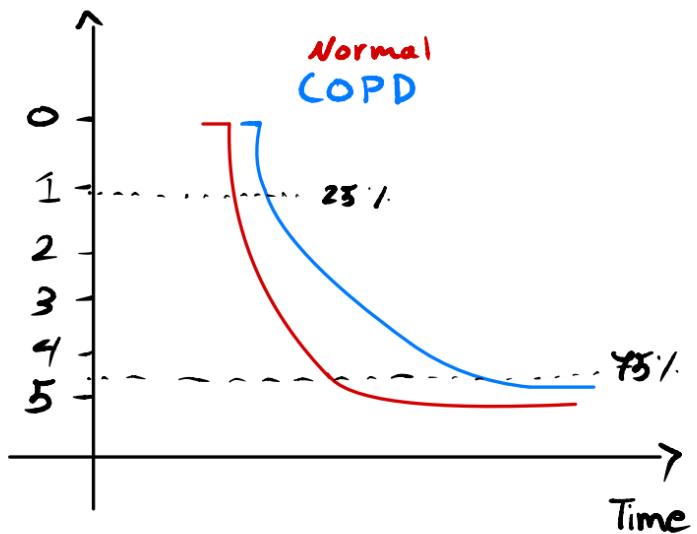
In patients with COPD, such as emphysema (blue curve), the lungs can be inflated but expiration is limited due to airflow obstruction. These patients start from a higher total lung capacity (TLC'), around 8 L, and their maximum expiratory flow rate is reduced. Because they cannot completely empty the lungs, the residual volume (RV) is increased, reaching around 2 L, and the flow–volume loop is shifted to the left.

In patients with a restrictive disease, the primary problem is not expiration. They may show normal or relatively higher expiratory flow rates at lung volumes comparable to the normal curve. These patients start from a lower total lung capacity (TLC), around 4 L, with a MEFR around 400 L/min (higher than the normal situation at the same volume), and end at a lower residual volume (RV), around 0.5 L. With this axis orientation, the flow–volume loop is shifted to the right.

All this information could be obtained with a single breath through the spirometer.

Testing the expiration of a patient with COPD, we can notice that the difficulty in expiration is more prominent during the middle of forced expiration. This means that the first 25% and the last 25% of the forced vital capacity (FVC) are relatively less affected in both normal and COPD conditions. Therefore, sensitive tests focus on measuring the middle 50% of the forced vital capacity. The following curve illustrates this, where in the middle portion of expiration, the expiratory flow rate may be around 3.5 L/s in a normal individual, compared with about 1.5 L/s in a patient with COPD.

Expired Volume (L)



Closing volume is a more sensitive test that will be discussed later.

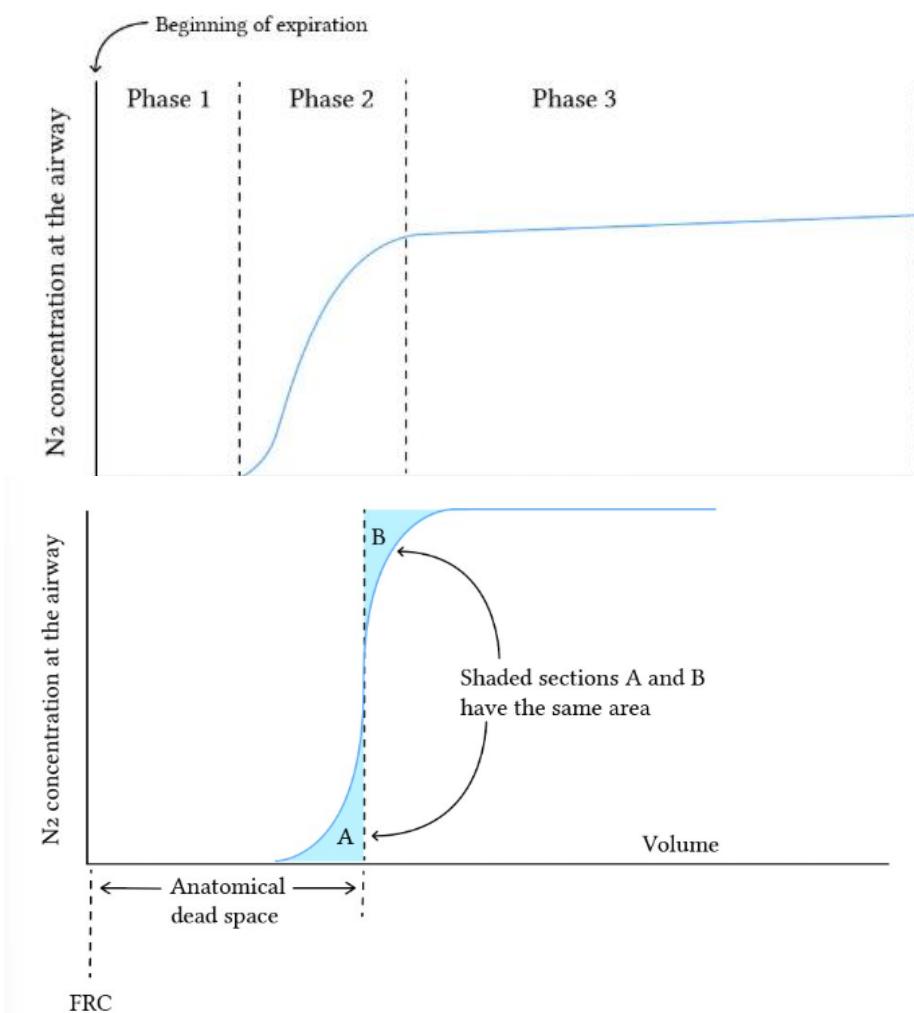
When studying lung zones, we identify the anatomical dead space and the alveolar zone. In addition, there is a transitional (mixing) zone between them, where dead space air mixes with alveolar air.

How to Measure the Anatomical Dead Space Volume

We ask a patient to inhale and then exhale, while analyzing the CO_2 concentration in the expired air. The composition of the anatomical dead space varies during the respiratory cycle: at the end of inspiration, it is similar to the composition of atmospheric air, whereas at the end of expiration, it resembles alveolar air.

When the percentage of CO_2 in expired air is plotted against expired volume, the initial expired volume contains no CO_2 (phase I), reflecting gas from the anatomical dead space. As expiration continues, the CO_2 concentration rises gradually as expired air becomes a mixture of dead space and alveolar gas (phase II), until a plateau is reached, representing pure alveolar gas (phase III). The dead space volume corresponds to the expired volume at the midpoint of phase II. If nitrogen is used instead of CO_2 , the subject must inhale 100% oxygen at the start of the manoeuvre, and the measurement then corresponds to the Fowler method for anatomical dead space.

The figures show N_2 concentration on the Y axis, the doctor drew the same figures using CO_2 concentration, same figure shape should be obtained in both situations.



When we breathe, the tidal volume (500 mL) is divided into 150 mL occupying the anatomical dead space and 350 mL reaching the alveoli. Multiplying these volumes by a respiratory rate of 12 breaths/min gives a dead space ventilation of 1.8 L/min and an alveolar ventilation of 4.2 L/min (close to the cardiac output). Thus, the respiratory minute ventilation of 6 L/min discussed previously does not correspond to alveolar ventilation, since a portion of the inspired air remains in the anatomical dead space.

Normally, for respiration to occur, both ventilation (V) and blood perfusion (Q) are required, with a normal V/Q ratio of approximately 0.84. In pathological conditions where the heart is weak and fails to adequately perfuse certain lung regions, such as the apical areas, these regions do not participate in gas exchange despite being ventilated.

These ventilated but non-perfused alveoli behave like dead space and are referred to as alveolar dead space, where the V/Q ratio approaches infinity because Q is zero. As a result, part of the 350 mL of alveolar ventilation becomes ineffective for gas exchange and is called alveolar wasted volume (AWV). Assuming an alveolar dead space volume of 50 mL, adding this to the anatomical dead space volume (ADSV) gives the physiological dead space volume (PDSV).

$$PDSV = ADSV + AWV$$

Normally the alveolar dead space volume is zero, so the physiological dead space volume will be equal the anatomical dead space. In summary, PDSV can be equal to or higher than ADSV but not lower than ADSV.

How to Measure the Physiological Dead Space Volume

The physiological dead space volume can be calculated using the following equation:

$$Physiological\ Dead\ Space\ Volume = V_T \times \left(\frac{P_aCO_2 - P_{\bar{E}}CO_2}{P_aCO_2} \right)$$

V_T : Tidal Volume, P_aCO_2 : Arterial CO_2 Partial Pressure,

$P_{\bar{E}}CO_2$: Mixed Expired Air CO_2 Partial Pressure

$$PDSV = 500\ ml \times \left(\frac{40\ mmHg - 28\ mmHg}{40\ mmHg} \right) = 150\ ml$$

$150\ ml = ADSV$, which means no alveolar wasted volume is present.

In pathological conditions where there is an alveolar wasted volume, $P_{\bar{E}}CO_2$ will be decreased as there is an amount of air that goes in and out without participating in CO_2 exchange. Assume $P_{\bar{E}}CO_2$ is 20 mmHg, PDSV will be equal to 250 ml, subtracting 150 ml (ADSV) from 250 ml gives us a 100 ml of alveolar wasted volume (AWV).

Changes from VERSION 0 to VERSION 1:

- “all-in-one” → “all-or-none” (in page **3**)
- Shifted the SABA test after explaining FEV_1/FVC ratio
- Added examples for SABAs (in page **3**)
- Right → left (last word in the first paragraph after the graph; page **5**)